PTO 09-3475

CC=JP
DATE=20011009
KIND=KOKAI
PN=2001276212

BLOOD COMPONENT COLLECTING METHOD AND BLOOD COMPONENT COLLECTING CIRCUIT
[KETSUEKI SEIBUN SAISHU HOHO OYOBI KETSUEKI SEIBUN SAISHU KAIRO]

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UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. MARCH 2009
TRANSLATED BY: SCHREIBER TRANSLATION,INC.

PUBLICATION COUNTRY	(10):	JP
DOCUMENT NUMBER	(11):	2001276212
DOCUMENT KIND	(12):	Kokai
PUBLICATION DATE	(43):	20011009
APPLICATION NUMBER	(21):	2000092916
APPLICATION DATE	(22):	20000330
INTERNATIONAL CLASSIFICATION	(51):	A61M 1/02 A61J 1/05
PRIORITY COUNTRY	(33):	N/A
PRIORITY NUMBER	(31):	N/A
PRIORITY DATE	(32):	N/A
INVENTOR(S)	(72):	Noboru Ishida
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DESIGNATED CONTRACTING STATES	(81):	N/A
TITLE	(54):	BLOOD COMPONENT COLLECTING METHOD AND BLOOD COMPONENT COLLECTING CIRCUIT
FOREIGN TITLE	[54A]:	KETSUEKI SEIBUN SAISHU HOHO OYOBI KETSUEKI SEIBUN SAISHU KAIRO

[What is Claimed is]

1. A blood component collecting method which uses a blood component collecting circuit comprising at least a whole blood collecting bag, a plasma collecting bag, an erythrocyte liquid collecting bag and a soft-housing type leukocyte-removing filter, characterized in that the blood component collecting method comprises the steps of: a centrifugation process where, once the whole blood has been collected in the whole blood collecting bag, the whole blood in the whole blood collecting bag is divided into the plasma component and the haemocyte liquid by centrifuging the blood component collecting circuit; a leukocyte-poor plasma collecting process where the plasma component in the whole blood collecting bag is passed through the leukocyte-removing filter and is collected in the plasma collecting bag; and a leukocyte-poor erythrocyte liquid collecting process where, after the leukocyte-poor plasma collecting process, the haemocyte liquid in the whole blood collecting bag is passed through the leukocyte-removing filter and is collected in the erythrocyte liquid collecting bag.

2. The blood component collecting method according to Claim 1, characterized in that an erythrocyte stock solution is

packed in the erythrocyte liquid collecting bag, the blood component collecting method comprises an erythrocyte stock solution infusion process after the leukocyte-poor plasma collecting process and before the leukocyte-poor erythrocyte liquid collecting process, where the erythrocyte stock solution in the erythrocyte liquid collecting bag is infused into the erythrocyte liquid in the whole blood collecting bag, and the erythrocyte stock solution-added leukocyte-poor erythrocyte liquid is collected in the leukocyte-poor erythrocyte liquid collecting process.

3. The blood component collecting method according to Claim 1 or 2, characterized in that the leukocyte-poor plasma collecting process is conducted while the plasma collecting bag is arranged below the leukocyte-removing filter.

4. A blood component collecting circuit which is used in the blood component collecting method according to any of Claims 1 through 3, characterized in that the blood component collecting circuit comprises a whole blood collecting bag, a plasma collecting bag, an erythrocyte liquid collecting bag, a connecting tube having a bifurcation of which the first end is connected to the

plasma collecting bag and the second end is connected to the erythrocyte liquid collecting bag, and a leukocyte-removing filter which is arranged between the connecting tube and the whole blood collecting bag.

5. The blood component collecting method according to Claim 4, characterized in that an erythrocyte stock solution is packed in the erythrocyte liquid collecting bag.

[Detailed Description of the Invention]

[0001]

[Technical Field of the Invention] The present invention relates to a method for collecting blood components and a blood component collecting circuit.

[0002]

[Prior Art] In recent years, instead of whole blood transfusion, blood component transfusion, in which only the required components in the blood is transfused into patients, and the plasma collecting for preparing plasma preparations have come to be conducted. Examples of such separate collection methods for blood include the methods disclosed in Japanese Examined Patent Publication No. H6-59304 and Japanese Examined Patent Publication No. H6-59305, wherein the blood collected in a blood collection bag is

first passed through a leukocyte-removing filter in order to remove leukocytes, and is then subjected to a centrifugation in order to collect the blood components separated due to the differences of the specific gravities. However, since the buffy coat component is removed by the filtration, the boundary surface between the upper plasma layer and the lower erythrocyte layer becomes unclear after the centrifugation, which allows erythrocyte to be mixed into the plasma when the plasma component is separated.

[0003] Further, Japanese Unexamined Patent Publication No. H6-197962 and Japanese Unexamined Patent Publication H4-200550 disclose a method wherein blood collected in a blood collecting bag is subjected to centrifugation and is passed through a leukocyte-removing filter, thereby collecting blood components. In Japanese Unexamined Patent Publication No. H4-200550, however, the plasma is not passed through the filter and, therefore, a large amount of leukocytes are contained in the resulting plasma preparation. The content can be as much as 2×10^7 in the plasma per 400 mL-blood collecting bag. In general, when a blood transfusion reaction attributed to the incorporation of leukocytes into the blood preparation is considered, since the content level of n (integer) $\times 10^6$ is considered to be the borderline which induces antibody formation, the

incorporation of leukocytes at a content level of higher than n (integer) $\times 10^6$ may reduce the safety of the blood transfusion. Further, part of erythrocytes may be mixed into the plasma during transportation. The content can be as much as 5×10^8 in the plasma per 400 mL-blood collecting bag. Since plasma preparations are usually stored frozen, the erythrocyte incorporated thereinto is hemolyzed and haemoglobin thereby floats in the plasma. The transfusion of a large amount of haemoglobin induces kidney disorders or the like, which causes a clinical problem. In Japanese Unexamined Patent Publication No. H6-197962 which uses a hard housing-type leukocyte-removing filter, the removal rate of leukocytes from the plasma component is not satisfactory. Hence, the present invention intends to provide a blood component collecting method, as well as a blood component collecting circuit used in the method, which solves the above-described problems and prevents the incorporation of erythrocytes and leukocytes when the components of the whole blood are separated, in particular, when the plasma component is separated.

[0004]

[Means of Solving the Problems] The blood component collecting method which achieves the above-described object is a method which uses a blood component collecting circuit

comprising at least a whole blood collecting bag, a plasma collecting bag, an erythrocyte liquid collecting bag and a soft-housing type leukocyte-removing filter, characterized in that the blood component collecting method comprises the steps of: a centrifugation process where, once the whole blood has been collected in the whole blood collecting bag, the whole blood in the whole blood collecting bag is divided into the plasma component and the haemocyte liquid by centrifuging the blood component-collecting circuit; a leukocyte-poor plasma collecting process where the plasma component in the whole blood collecting bag is passed through the leukocyte-removing filter and is collected in the plasma collecting bag; and a leukocyte-poor erythrocyte liquid collecting process where, after the leukocyte-poor plasma collecting process, the haemocyte liquid is in the whole blood collecting bag is passed through the leukocyte-removing filter and is collected in the erythrocyte liquid collecting bag.

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Further, it is preferred that an erythrocyte stock solution is packed in the erythrocyte liquid collecting bag, the blood component collecting method comprises an erythrocyte stock solution infusion process after the leukocyte-poor plasma collecting process and before the leukocyte-poor

erythrocyte liquid collecting process, where the erythrocyte stock solution in the erythrocyte liquid collecting bag is infused into the erythrocyte liquid in the whole blood collecting bag, and the erythrocyte stock solution-added leukocyte-poor erythrocyte liquid is collected in the leukocyte-poor erythrocyte liquid collecting process. Further, it is preferred that the leukocyte-poor plasma collecting process is conducted while the plasma collecting bag is arranged below the leukocyte-removing filter.

[0005] Further, the blood component collecting circuit which achieve the above-described object is a blood component collecting circuit which is used in the above-described blood component collecting method and is characterized in that the blood component collecting circuit comprises a whole blood collecting bag, a plasma collecting bag, an erythrocyte liquid collecting bag, a connecting tube having a bifurcation of which the first end is connected to the plasma collecting bag and the second end is connected to the erythrocyte liquid collecting bag, and a leukocyte-removing filter which is arranged between the bifurcation of the connecting tube and the whole blood collecting bag. Further, it is preferred that an

erythrocyte stock solution is packed in the erythrocyte liquid collecting bag.

[0006]

[Modes of Implementing the Invention] The inventive blood component collecting method and blood component collecting circuit are described with reference to embodiments shown in diagrams. Fig. 1 is an outline drawing of a blood component collecting circuit for the blood component collecting method in an embodiment according to the present invention. The inventive blood component collecting method uses a blood component collecting circuit 1 comprising at least a whole blood collecting bag 2, a plasma collecting bag 3, an erythrocyte liquid collecting bag 4 and a soft-housing type leukocyte-removing filter 5. The blood component collecting method comprises the steps of: a centrifugation process where, once the whole blood has been collected in the whole blood collecting bag 2, the whole blood in the whole blood collecting bag 2 is divided into the plasma component and the haemocyte liquid by centrifuging the blood component collecting circuit 1; a leukocyte-poor plasma collecting process where the plasma component in the whole blood collecting bag 2 is passed through the leukocyte-removing filter 5 and is collected in the plasma collecting bag 3; and a leukocyte-poor

erythrocyte liquid collecting process where, after the leukocyte-poor plasma collecting process, the haemocyte liquid in the whole blood collecting bag 2 is passed through the leukocyte-removing filter 5 and is collected in the erythrocyte liquid collecting bag 4.

[0007] Further, the inventive blood component collecting circuit 1 comprises a whole blood collecting bag 2, a plasma collecting bag 3, an erythrocyte liquid collecting bag 4, a connecting tube 10 having a bifurcation 13 of which the first end is connected to the plasma collecting bag 3 and the second end is connected to the erythrocyte liquid collecting bag 4, and a leukocyte-removing filter 5 which is arranged between the connecting tube 10 and the whole blood collecting bag 2. The connecting tube 10 comprises tubes 11, 12, 14 and 15, and a bifurcation 13. Further, an erythrocyte stock solution (not shown) can be packed in the erythrocyte liquid collecting bag 4, the blood component collecting method can comprise an erythrocyte stock solution infusion process after the leukocyte-poor plasma collecting process and before the leukocyte-poor erythrocyte liquid collecting process, where the erythrocyte stock solution in the erythrocyte liquid collecting bag 4 is infused into the erythrocyte liquid in the whole blood collecting bag 2, and the erythrocyte stock

solution-added leukocyte-poor erythrocyte liquid can be collected in the leukocyte-poor erythrocyte liquid collecting process.

[0008] In the embodiment shown in Fig. 1, the whole blood collecting bag 2 is formed by assembling two sheets and fusing (e.g., heat fusing and high-frequency fusing) or adhering the periphery of the assembled sheets into a bag. A storage space for the collected blood is formed in the inner space enclosed by the sealed portion. An anticoagulant, such as heparin sodium liquid, ACD-A liquid, CPD liquid and CPDA liquid, is packed in the storage space in advance. The whole blood collecting bag 2 is connected to a blood incurrent port 5a of the leukocyte-removing filter 5 via the tube 11. The tube 11 is provided with a tearable communicating member 23 which prevents the anticoagulant in the blood collecting bag from shifting to a plasma component collecting container before blood transfusion. A blood-collecting means 7 is provided on the upper portion of the whole blood collecting bag 2. The blood-collecting means 7 comprises a blood collecting needle 21 and a tube 22 which introduces the collected blood from the blood collecting needle 21 into the storage area. Further, an opening 2a for suspension feeding is provided on the bottom portion of the whole blood

collecting bag 2, whereby the whole blood collecting bag 2 can be suspended in such a way that the upper portion can be arranged downwardly. The soft resins that can be used for a housing 30 in the leukocyte-removing filter 5 can also be used to constitute the whole blood collecting bag 2 so that the bag can be compressed.

[0009] The erythrocyte liquid collecting bag 4 can be formed in the same manner as the whole blood collecting bag 2 and has a storage space inside. Erythrocyte stock solutions, such as MAP liquid and SAGM liquid, can be packed in advance in the storage space in the erythrocyte liquid collecting bag 4. The erythrocyte liquid collecting bag 4 is connected to an excurrent blood section 44 (blood excurrent port 5b) of the leukocyte-removing filter 5 via the tubes 12 and 14. The tube 14 is provided with a tearable communicating member 24 which prevents the erythrocyte stock solution from shifting to other bags. Further, two tube openings which have been openably sealed by peel tabs are provided on the upper portion. These openings allow infusion needles to be inserted when the separated erythrocyte component is infused. Further, an opening 4a for suspension feeding is provided on the bottom portion of the erythrocyte liquid collecting bag 4.

The soft resins that can be used for the housing in the leukocyte-removing filter 5 can also be used to constitute the erythrocyte liquid collecting bag 4 so that the bag can be compressed.

[0010] The plasma collecting bag 3 can be formed in the same manner as the whole blood collecting bag 2, has a storage space inside, and is usually empty before plasma is held therein. The plasma collecting bag 3 is connected to a blood excurrent port 5b of the leukocyte-removing filter 5 via the tubes 15 and 12. Further, tube openings which have been openably sealed by peel tabs are provided on the upper portion of the plasma collecting bag 3. These openings allow infusion needles to be inserted when the separated plasma component is infused. Further, an opening 3a for suspension feeding is provided on the bottom portion of the plasma collecting bag 3. The soft resins that can be used for the housing in the leukocyte-removing filter 5 can also be used to constitute the plasma collecting bag 3 so that the bag can be pushed. In the present embodiment, a three-way connector is used as a bifurcation 13 but is not restricted to it; a three-way cock can also be used as the bifurcation. In addition, the bifurcation can also be formed by splitting a tube three ways.

[0011] Preferred examples of materials for the production of tubes 22, 11, 12, 14 and 15 include polyesters, such as polyvinyl chloride, polyethylene, polypropylene, PET and PBT, and thermoplastic elastomers, such as ethylene/vinyl chloride copolymer, polyurethane, polyester elastomer, and styrene/butadiene/styrene copolymer. In addition, it is preferred that the bifurcation 13 is formed of the same resin as the blood incurrent port 5a and the blood excurrent port 5b, which are described later.

[0012] The leukocyte-removing filter 5 used herein is a soft housing type. As shown in Fig. 2 to Fig. 5, a soft resin bag-like housing 30 comprises two thermoplastic soft resin sheets 31 and 32, with the sheet 31 being arranged on the side of the incurrent blood section 43 and the sheet 31 being arrange on the side of the excurrent blood section 44. The inner face 30a of the sheet 32 on the excurrent side, i.e., the face which faces the excurrent blood section 44 of the leukocyte-removing filter 5, has an irregularity 33 having a vertical interval of 0.2 to 2 mm. By providing irregularity 33 on the inner face 30a of the sheet 32 on the excurrent side, when the inner face 30a of the soft resin bag-like housing 30 (i.e., the inner face 30a of the sheet 32 on the excurrent side) is compressed by the leukocyte-removing filter 5, the close contact of both

faces can be prevented, thereby ensuring the passage between the leukocyte-removing filter 5 and the inner face of the housing 30a (i.e., the inner face of the sheet 32 on the excurrent side) and preventing the decrease in the filtration rate.

[0013] In the leukocyte-removing filter 5, the leukocyte-removing filter member 35 comprises a sheet-like thermoplastic soft resin frame 51 and a filtrate member 52, of which the periphery is directly or indirectly adhered to the frame 51. The filtrate member 52 is formed of a lamination of multiple filters. The leukocyte-removing filter member 35 used herein comprises a filtrate portion which is constituted of the filtrate member 52, and a non-filtrate portion which is provided on the entire periphery of the filtrate portion. The leukocyte-removing filter member 35 is inserted between two thermoplastic soft resin sheets, and the periphery of the sheet-like thermoplastic soft resin frame 51 is fused into these thermoplastic soft resin sheets. Therefore, the leukocyte-removing filter member 35 divides the space (in the housing 30) created by the two thermoplastic soft resin sheets 31 and 32 into the incurrent blood section 43 and the excurrent blood section 44.

[0014] The soft resin tube that constitutes the blood incurrent port 5a is fused into the central portion of one end (upper end) of the two thermoplastic soft resin sheets in such a way that the soft resin tube can be connected to the incurrent blood section 43, i.e., the one opening of the soft resin tube can be opened within the incurrent blood section 43. Similarly, the soft resin tube that constitutes the blood excurrent port 5b is fused into the central portion of the other end (lower end) of the two thermoplastic soft resin sheets in such a way that the soft resin tube can be connected to the excurrent blood section 44, i.e., the opening of the soft resin tube can be opened within the excurrent blood section 44.

[0015] Further, the blood incurrent port 5a and the blood excurrent port 5b are connected to the tube 11, which feeds filtrated substances (not shown) to the leukocyte-removing filter, and the tube 12, which discharges the filtrate. As a result, the tube 11 is connected to the incurrent blood section 43 via the blood incurrent port 5a, and the tube 12 is connected to the excurrent blood section 44 via the blood excurrent port 5b. The connection of the tubes 11 and 12 to the blood incurrent port 5a and the blood excurrent port 5b, respectively, can be conducted by inserting the tubes 11 and 12 into the soft tubes which constitute the

ports 5a and 5b, respectively, and fusing the resulting tubes. For this reason, the external diameter of the tubes is preferably generally the same as the internal diameter of the ports. Preferred examples of materials for the production of the tubes include resins that can be readily fused into the blood incurrent port 5a and the blood excurrent port 5b. In particular, the same or the same system resins as the resins to be used for the blood incurrent port 5a and the blood excurrent port 5b are preferred.

[0016] The adhesion of the thermoplastic soft resin sheets 31 and 32, the sheet-like thermoplastic soft resin frame 51 in the leukocyte-removing filter member 35, the blood incurrent port 5a and the blood excurrent port 5b that constitute the housing 30 can be conducted by fusing, which does not require an adhesive agent. The welding can be external welding by heat-sealing, or internal welding, such as high-frequency welding and ultrasonic welding. The welding can be conducted by simultaneously fusing the above-mentioned portions or by stepwisely fusing the portions.

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The filtrate member 52 in the leukocyte-removing filter 35 is a laminate of multiple filters constituted of porous

materials or non-woven fabric. The desired number of laminations of the filters is 2 to 10.

[0017] The term "porous material" to be used in the filtrate member 52 refers to a liquid-permeable structure having many micropores which allows one face to communicate to the other face; known examples of such porous materials include porous materials constituted of natural, synthetic, semisynthetic or regenerated organic/inorganic fibers, organic/inorganic porous materials, such as sponge forms, porous materials, of which the pores are formed by eluting, sintering, expanding or perforating pore components, and porous materials obtained by packing or conjugating organic/inorganic particles. Of these, particularly preferred examples of the materials for the filtrate member (filters) 52 of the leukocyte-removing filter member 35 include sponge-like polyurethane porous materials and polyvinyl formal porous materials. Regarding the pore size of such porous materials, in the case of using porous materials having a large pore size, a thick porous material can be used or thin porous materials can be laminated, and in the case of using porous materials having a small pore size, a thin porous material can be used straightforwardly. Any porous materials can be used as long as they allow blood cells to be passed through by appropriately adjusting

the pore size and thickness. In particular, the use of a porous material having an average pore size of 5 to 20 μm is effective at removing leukocytes.

[0018] Flexible thermoplastic resins can be used for the production of the thermoplastic soft resin sheets 31 and 32, the sheet-like thermoplastic soft resin frame 51 in the leukocyte-removing filter member 35, the blood incurrent port 5a and the blood excurrent port 5b that constitute the housing 30; specific examples of such flexible thermoplastic resins include: thermoplastic elastomers, such as soft vinyl chloride resins (polyvinyl chloride, vinyl chloride/vinyl acetate copolymer, vinyl chloride/ethylene copolymer, vinyl chloride/vinylidene chloride copolymer, polyvinyl chloride/urethane copolymer, polyvinyl chloride/acrylonitrile copolymer, vinyl chloride/methyl methacrylate copolymer and soft polyvinyl chloride variants constituted of these polymers and plasticizers), hydrogenated matter of styrene/butadiene/styrene and hydrogenated matter of styrene/isoprene/styrene copolymer; and mixtures of thermoplastic elastomers and a softener, such as polyolefin and ethylene/ethyl acrylate; polyurethanes (polyester-based polyurethane and polyether-based polyurethane); polyolefins (mixtures of polyethylene, polypropylene, ethylene/propylene copolymer, ethylene/vinyl

acetate copolymer and polypropylene and polyethylene or polybutene); polyesters (polyethylene terephthalate and polybutylene terephthalate); and polyamides. Of these, particularly preferred examples include soft vinyl chloride resins, styrene/butadiene/styrene copolymer, polyester, styrene/ethylene/butylene/styrene copolymer and thermoplastic elastomers comprising essentially these polymers.

[0019] Hard resins can also be used for the production of the blood incurrent port 5a and the blood excurrent port 5b. Examples of such hard resins include hard or semi-hard vinyl chloride, polycarbonate, acryl resins and styrene resins. The above-described blood component collecting circuit 1 can be used for collecting blood components by installing it, for example, in a blood component separation apparatus as shown in Japanese Patent No. 2547636. The blood component separation apparatus is not restricted to the above-mentioned apparatus. In addition, the blood component collecting circuit can also be used by using a drop system, which does not require a blood component separation apparatus.

[0020] Next, the case where blood component separating apparatus in the inventive blood component collecting method is described below as an example. First, the whole

blood is collected in the whole blood collecting bag 2 by a blood-collecting means 7. After collection of the blood, the root of a tube 22 is sealed by using a tube sealer and the blood-collecting means 7 is then removed. Next, the blood component collecting method 1 is installed in a centrifugal separator and is then subjected to a centrifugation. The centrifuged whole blood in the whole blood collecting bag 2 is divided into the plasma layer which consists mainly of plasma in the upper portion of the bag 2 and the erythrocyte layer which consists mainly of erythrocytes in the lower portion of the bag 2. Depending on the degree of centrifugation, leukocytes are generally mixed into the upper plasma layer and are also mixed into the erythrocyte layer. If the amount of the leukocytes in the plasma and erythrocyte liquid in the 400 mL blood collecting bag is $n \times 10^6$, antibody formation may be induced, which is not preferred.

[0021] Next, the leukocyte-poor plasma collecting process is conducted, wherein the plasma layer separated in the whole blood collecting bag 2 by the above centrifugation process is passed through the leukocyte-removing filter 5 and is then collected in the plasma collecting bag 3. While the leukocyte-removing filter 5 is stood up such that the blood incurrent port 5a is arranged downwardly and the

blood excurrent port 5b is arranged upwardly, the whole blood collecting bag 2 is held in the holding compartment of the blood component separating apparatus (not shown) arranged at a position lower than the leukocyte-removing filter 5, the plasma collecting bag 3 is arranged at a position lower than the leukocyte-removing filter 5, and the erythrocyte liquid collecting bag 4 is hung at a position higher than the leukocyte-removing filter 5. The plasma layer in the upper portion of the whole blood collecting bag 2 is sent to the plasma collecting bag 3 by compressing the whole blood collecting bag 2. The plasma passes though the leukocyte-removing filter 5, at which leukocytes are removed, and flows into the plasma collecting bag 3. The boundary surface between the plasma layer and the erythrocyte layer in the bag is gradually elevated as the compression continues, and the compression is terminated when the interface of the erythrocyte layer is detected at a liquid detection part (not shown) in the blood component-separating apparatus. The plasma remains at the inlet or outlet of the filter 5, but most of the remaining plasma is collected in the plasma collecting bag 3 because the plasma collecting bag 3 is arranged at a position lower than the leukocyte-removing filter 5. After separation, the tube 15 is sealed by using a tube sealer

and the plasma collecting bag 3 is removed, thereby yielding a plasma preparation-containing bag.

[0022] Further, since the plasma component passes through the leukocyte-removing filter 5 during separation, an additional air-removing process can be omitted.

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Further, the leukocyte-poor plasma collecting process where this plasma layer is collected in the plasma collecting bag 3 though the leukocyte-removing filter 5 can be preferably conducted without compressing the filter 5 (in particular, without compressing the incurrent blood section 43 of the filter). As a result, the incurrent blood section 43 of the filer 5 can be blown up, whereby the force which pushes liquid components in the filer can be reduced, the filtration flow rate can be reduced, and the leukocyte-removing performance can be improved (in general, the filtration flow rate and the leukocyte-removing performance are in an inverse correlation). Further, the plasma with a small amount of floating erythrocytes also remains in the incurrent blood section 43 of the filter 5 due to the decreased filtration flow rate. As a result, the plasma, which can be readily passed through the filter, can selectively pass through while erythrocytes are caught by the filter and removed.

[0023] Next, after the leukocyte-poor plasma collecting process and before the leukocyte-poor erythrocyte liquid collecting process, an erythrocyte stock solution infusion process is conducted, wherein the erythrocyte stock solution in the erythrocyte liquid collecting bag 4 is infused into the erythrocyte liquid in the whole blood collecting bag 2. A connecting means 24 provided with the tube 14 which is connected to the erythrocyte liquid collecting bag 4 is folded to transport the erythrocyte stock solution (MAP) to the whole blood collecting bag 2 via the leukocyte-removing filter 5, thereby mixing the erythrocyte stock solution (MAP) into the haemocyte liquid in the whole blood collecting bag 2. In this case, the erythrocyte liquid collecting bag 4, the leukocyte-removing filter 5 and the whole blood collecting bag 2 are arranged in such an order from top. As a result, the erythrocyte stock solution in the erythrocyte liquid collecting bag 4 can be transported to the whole blood collecting bag 2 without allowing the erythrocyte stock solution to remain in the leukocyte-removing filter 5.

[0024] Next, a leukocyte-poor erythrocyte liquid collecting process is conducted, wherein the haemocyte liquid in the whole blood collecting bag 2 is passed through the leukocyte-removing filter 5 and is collected in the

erythrocyte liquid collecting bag 4. In the present embodiment, the whole blood collecting bag 2, the leukocyte-removing filter 5, and the erythrocyte liquid collecting bag 4 are separated from the blood component separating apparatus, and arranged in such an order from top, whereby the erythrocyte liquid in the whole blood collecting bag 2 can fed to the leukocyte-removing filter 5 for filtration. Thereafter, once the erythrocyte liquid has been collected in the erythrocyte liquid collecting bag 4, the tube 14 is sealed by using a tube sealer and the erythrocyte liquid collecting bag 4 is removed, thereby yielding an erythrocyte stock solution-containing concentrated erythrocyte preparation-containing bag.

[0025] In the present invention, the erythrocyte stock solution infusion process is conducted before the leukocyte-poor erythrocyte liquid is collected in the erythrocyte liquid collecting bag, but is not restricted thereto; the leukocyte-poor erythrocyte liquid can also be collected in the erythrocyte liquid collecting bag (the bag can be optionally filled with the erythrocyte stock solution) without conducting the erythrocyte stock solution infusion process. Further, in the above-described overall blood component-collecting circuit, the whole blood collecting bag, the plasma collecting bag, the erythrocyte

liquid collecting bag and the leukocyte-removing filter are not necessarily completely connected via tubes to form a circuit, i.e., one or more parts can be unconnected and can be connected before use by using an aseptic connecting device.

[0026] (Experiment 1)

(Embodiment 1) The blood component-collecting circuit having the above-described structure as shown in Fig. 1 was used. 400 mL of the whole blood was collected in a whole blood collecting bag constituted of soft vinyl chloride resin, and was then subjected to a centrifugation. As a result, the whole blood was divided into an upper plasma layer and a lower erythrocyte layer in the whole blood collecting bag. Thereafter, while a plasma collecting bag was arranged at a position lower than a soft leukocyte-removing filter, the whole blood collecting bag was compressed so that the plasma component separated in the whole blood collecting bag could be passed through the soft leukocyte-removing filter and collected in a plasma collecting bag. The erythrocyte stock solution in an erythrocyte liquid collecting bag was infused into the erythrocyte liquid in the whole blood collecting bag. Thereafter, the erythrocyte stock solution-containing erythrocyte liquid was passed through the soft leukocyte-

removing filter and collected in the erythrocyte liquid collecting bag.

[0027] The leukocyte-removing filter comprised, as housing-forming members, a soft polyvinyl chloride sheet, having a length of 110 mm, a width of 75 mm, a height of 0.4 mm and a satin surface, which was arranged on the blood incurrent side, and a soft polyvinyl chloride sheet having a length of 110 mm, a width of 75, a height of 0.4 mm, and ribs having a height of 0.8 mm, a bottom length of 1 mm and a cross-section being generally triangle provided in the longitudinal direction at an interval of 2 mm, which was arranged on the excurrent side. A blood incurrent port and a blood excurrent port were soft polyvinyl chloride tubes (length: 23 mm; internal diameter: 4 mm; external diameter: 6 mm) formed by injection molding. A leukocyte-removing filter was prepared by laminating 6 polyurethane porous materials (thickness: approximately 1 mm; average pore size: 5 μm; length: approximately 85 mm; width: approximately 65 mm) punched into an oval shape, and heat-sealing the outer periphery of the resulting laminate. This leukocyte-removing filter had a thickness of the sealed outer periphery of 1 mm and a thickness of non-sealed portion of approximately 10 mm. A sheet-like frame (length: 110 mm; width: 75 mm; frame width: 10 to 25 mm; thickness:

0.4 mm) was prepared by a sheet formed of a 1/1 mixture resin of a polyurethane resin and a polyvinyl chloride resin, with the size of the cut-off portion inside the film being slightly smaller than the above-mentioned filter. The leukocyte-removing filter member was prepared by applying the sheet-like frame to the leukocyte-removing filer and externally fusing the entire outer periphery of the leukocyte-removing filter and the entire inner periphery of the sheet-like frame.

[0028] The soft polyvinyl chloride sheet on the blood

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incurrent side was arranged downwardly, the leukocyte-removing filter member to which the filers had been fused was placed on the soft polyvinyl chloride sheet, and the soft polyvinyl chloride tube was arranged between the extension portion on the upper portion of the sheet-like frame of the leukocyte-removing filter member and the soft polyvinyl chloride sheet on the blood incurrent side. Thereafter, the soft polyvinyl chloride sheet on the blood excurrent side was placed on the leukocyte-removing filter member such that the face with ribs could be made to make contact with the leukocyte-removing filter member, the soft polyvinyl chloride tube was arranged between the extension portion on the lower portion of the sheet-like frame of the

leukocyte-removing filter member and the soft polyvinyl chloride sheet on the blood excurrent side, and the periphery of the resulting assembly was fused by high-frequency welding. Finally, unnecessary portion was removed by a punch, thereby yielding the inventive leukocyte-remover.

[0029] (Embodiment 2) An embodiment was obtained by the same method as Embodiment 1, except that the plasma collecting bag was not placed at a position lower than the soft leukocyte-removing filter during collecting the plasma, and once the collection of the plasma had been completed, the soft leukocyte-removing filter was lifted to be placed at a position higher than the plasma collecting bag, and the plasma in the filter was sent to the plasma collecting bag by compressing the soft leukocyte-removing filter.

[0030] (Embodiment 3) An embodiment was obtained by the same method as Embodiment 1, except that in the blood component collecting circuit, an erythrocyte liquid collecting bag that was not filled with an erythrocyte stock solution was used, and after the collection of the plasma in the plasma collecting bag, the erythrocyte liquid in the whole blood collecting bag was passed through the soft leukocyte-removing filter and collected in the plasma collecting bag.

[0031] (Embodiment 4) An embodiment was obtained by the same method as Embodiment 3, except that the plasma collecting bag was not placed at a position lower than the soft leukocyte-removing filter during collecting the plasma, and once the collection of the plasma had been completed, the soft leukocyte-removing filter was lifted to be placed at a position higher than the plasma collecting bag, and the plasma in the filter was sent to the plasma collecting bag by compressing the soft leukocyte-removing filter.

[0032] (Comparative Example 1) As shown by a blood component collecting circuit 50 in Fig. 6, in the same manner as Embodiment 1, except that the position of the soft leukocyte-removing filter was different from the blood component collecting circuit shown in Fig. 1, 400 mL of the whole blood collected in the whole blood collecting bag constituted of a soft vinyl chloride resin was subjected to a centrifugation. Thereafter, the plasma component divided in the whole blood collecting bag was collected in the plasma collecting bag. The erythrocyte stock solution in an erythrocyte liquid collecting bag was infused into the erythrocyte liquid in the whole blood collecting bag. Thereafter, the erythrocyte stock solution-containing erythrocyte liquid was passed through the soft leukocyte-

removing filter and collected in the erythrocyte liquid collecting bag.

[0033] (Comparative Example 2) As shown by a blood component collecting circuit 60 in Fig. 7, in the same manner as Embodiment 1, except that a blood component collecting circuit having a hard leukocyte-removing filter 65 and a bypass line 16 for the hard filter was used, 400 mL of the whole blood collected in the whole blood collecting bag constituted of a soft vinyl chloride resin was subjected to a centrifugation. Thereafter, the plasma component divided in the whole blood collecting bag was collected in the plasma collecting bag through the hard leukocyte-removing filter. The erythrocyte stock solution in an erythrocyte liquid collecting bag was infused into the erythrocyte liquid in the whole blood collecting bag. Thereafter, the erythrocyte stock solution-containing erythrocyte liquid was passed through the hard leukocyte-removing filter and collected in the erythrocyte liquid collecting bag. The hard leukocyte-removing filter used comprised, as a housing-forming member, a polycarbonate container having a length of 95 mm, a width of 70 mm and a thickness of 13 mm. A blood incurrent port and a blood excurrent port used were soft polyvinyl chloride resin tubes (length: 23 mm; internal diameter: 4 mm; external

diameter: 6 mm) formed by injection molding. The same leukocyte-removing filter as Embodiment 1 was used.

[0034] Data of the degree of contamination of cell components in the collected plasma and the operation time in Embodiments 1 to 4 and Comparative Examples 1 and 2 are shown in Table 1.

[0035]

[Table 1]

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	Collected amount of plasma (mL)	Total counts of leukocytes in plasma ($\times 10^6$)	Total counts of erythrocyte in plasma ($\times 10^7$)	Operating time for collecting plasma (min)
Embodiment 1	273 ± 18	0.7 ± 0.2	1.5 ± 0.7	0.6 ± 0.2
Embodiment 2	268 ± 20	0.7 ± 0.2	1.4 ± 0.8	1.8 ± 0.5
Embodiment 3	273 ± 19	0.7 ± 0.2	1.6 ± 0.8	0.6 ± 0.2
Embodiment 4	279 ± 18	0.7 ± 0.2	1.5 ± 0.9	1.9 ± 0.6
Comparative Example 1	280 ± 22	11.8 ± 5.2	28.2 ± 12.6	0.6 ± 0.2
Comparative Example 2	276 ± 19	3.4 ± 1.3	9.1 ± 3.7	1.7 ± 0.5

(n=5; average ± standard deviation)

Each haemocyte was counted using Sysmex XE2100, and the count of leukocytes at $\times 10^6$ level was conducted by Nageotte method.

[0036]

[Effect of the Invention] The blood component-collecting method according to the present invention is a method which uses a blood component-collecting circuit comprising at least a whole blood collecting bag, a plasma collecting bag, an erythrocyte liquid collecting bag and a soft-housing

type leukocyte-removing filter, characterized in that the blood component-collecting method comprises the steps of: a centrifugation process where, once the whole blood has been collected in the whole blood collecting bag, the whole blood in the whole blood collecting bag is divided into the plasma component and the haemocyte liquid by centrifuging the blood component-collecting circuit; a leukocyte-poor plasma collecting process where the plasma component in the whole blood collecting bag is passed through the leukocyte-removing filter and is collected in the plasma collecting bag; and a leukocyte-poor erythrocyte liquid collecting process where, after the leukocyte-poor plasma collecting process, the haemocyte liquid in the whole blood collecting bag is passed through the leukocyte-removing filter and is collected in the erythrocyte liquid collecting bag. Therefore, a plasma component in which almost no erythrocytes and leukocytes are contained can be collected.

[0037] Further, the blood component-collecting circuit according to the present invention is a blood component-collecting circuit which is used in the above-described blood component-collecting method and is characterized in that the blood component-collecting circuit comprises a whole blood collecting bag, a plasma collecting bag, an erythrocyte liquid collecting bag, a connecting tube having

a bifurcation of which the first end is connected to the plasma collecting bag and the second end is connected to the erythrocyte liquid collecting bag, and a leukocyte-removing filter which is arranged between the bifurcation of the connecting tube and the whole blood collecting bag.

[Brief Description of the Drawings]

[Fig. 1] Outline drawing of a blood component-collecting circuit in an embodiment according to the present invention.

[Fig. 2] Front view of a leukocyte-removing filter used in the blood component-collecting circuit according to the present invention as seen from the side of the blood excurrent section.

[Fig. 3] Rear view of the leukocyte-removing filter shown of Fig. 2.

[Fig. 4] Enlarged cross-sectional view of the leukocyte-removing filter of Fig. 2 taken along the line of A-A.

[Fig. 5] Cross-sectional view of the leukocyte-removing filter of Fig. 2 taken along the line of B-B.

[Fig. 6] Outline drawing of a comparative example blood component-collecting circuit.

[Fig. 7] Outline drawing of a comparative example blood component-collecting circuit.

[Reference Numerals]

1 - blood component collecting circuit

2 - whole blood collecting bag

3 - plasma collecting bag

4 - erythrocyte liquid collecting bag

5 - leukocyte-removing filter

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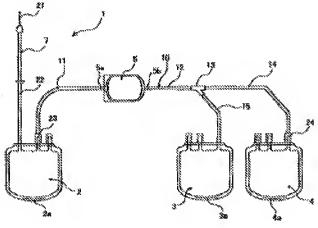
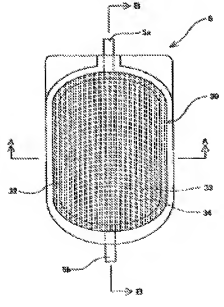
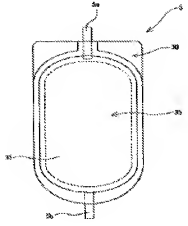
[Fig. 1]



[Fig. 2]



[Fig. 3]



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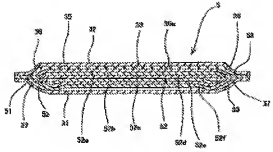
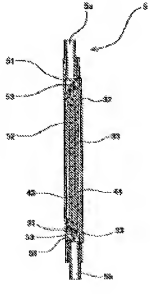
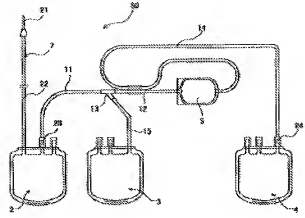
[Fig. 4]



[Fig. 5]



[Fig. 6]



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[Fig. 7]